

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: Terrell

Examiner: Brian J. Davis

Filed: August 20, 2003

Art Unit: 1621

Serial No.: 10/644,500

For: Method for the Preparation of Sevoflurane

**37 C.F.R. 1.132 Declaration**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, Ross C. Terrell, declare:

1. That I am a researcher at Minrad Inc. (retired Vice President of Research); and I have conducted research on the effect of chlorine substituent position on the efficiency of exchange of fluorine for chlorine in chloroethers.

2. That I understand that the above-referenced patent application recites claims directed to a method for preparing sevoflurane from sevochlorane and amine hydrofluorides and that these claims have been rejected based on references in light of which the Examiner asserts that the foregoing reaction is obvious. As a researcher in the field of haloethers, it is my opinion that the efficient reaction of  $(\text{CF}_3)_2\text{CHOCH}_2\text{Cl}$  with amine hydrofluorides to give sevoflurane is surprising.

That in the following reactions:

1.  $\text{CF}_3\text{CHClOCHF}_2 + \text{KF} \rightarrow \text{CF}_3\text{CHFOCHF}_2$
2.  $(\text{CF}_3)_2\text{CHOCHCl}_2 + \text{NaF} \rightarrow (\text{CF}_3)_2\text{CHOCHF}_2$
3.  $(\text{CF}_3)_2\text{CHOCH}_2\text{Cl} + \text{KF} \rightarrow (\text{CF}_3)_2\text{CHOCHF}_2$

the chlorine is "nucleophilically" substituted as it is well known that these NaF and KF reactions are nucleophilic reactions, and that based on the disclosure in the Muffler patent, one would expect these reactions to proceed efficiently with amine hydrofluorides instead of sodium or potassium fluoride.

4. That the chloroethers in examples 1 and 2, do not, in fact, react with amine hydrofluorides to give the expected products, and thus, of the above 3 reactions, all of which should react based on the criteria outlined in the Muffler patent and the U.S. Patent, only one does react.

5. That it is thus my opinion that the efficient reaction of sevochlorane with amine hydrofluorides to give sevoflurane is thus not obvious.

6. That all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 101 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued there from.

011474/00291 BFLDOCS 1717810v1

Respectfully submitted,



Ross C. Terrell, Ph.D.

Nov 16, 2006

Date